REMARKS

Claims 1-27 and 31-36 are pending. The amendments are fully supported by the original disclosure and, thus, no new matter is added by their entry. For example, informalities in claims 11 and 14 are corrected. Support for claim 34 may be found, inter alia, at page 3, lines 22-23, of the specification. The new claims are directed to the elected invention and should be examined in this application.

Species Election and Withdrawal of Claims

It was alleged on page 3 of the Office Action that claims 6-7 was drawn to a non-elected species. Therefore, the Examiner withdrew claims 6-7 from consideration. But specific bacteriophage listed in claims 6-7 are drawn to the elected elected species (i.e., a staphylococcal bacteriophage). Although only claim 2 recites staphylococcal bacteriophage, the withdrawn claims in fact do read on the elected species because the claims refer to specific types of staphylococcal bacteriophage. Thus, for example, phage 53 (recited in claim 6) and phage 75 (recited in claim 7) are both staphylococcal bacteriophage (see page 6, line 15, of the specification). Therefore, it is respectfully submitted that claims 6 and 7 should be examined in this application.

Rejoinder of the withdrawn method claims is also requested upon an indication that the elected product claims are allowable.

Information Disclosure Statement

It was alleged on Form PTO/SB/08a that the document Caldas et al. (Comptes Rendus 278:2369-2372, 1974) was not considered because "No explanation of relevance [was] provided." But this allegation is incorrect. Caldas et al. was cited in the Int'l Search Report (ISR) provided with the Information Disclosure Statement. The ISR cites this foreign-language document and provides the required concise explanation of relevance. See M.P.E.P. § 609.04(a) III ("the requirement for a concise explanation of relevance can be satisfied by submitting an English-language version of the search report or action which indicates the degree of relevance found by the foreign office" emphasis added).

Therefore, the return of an initialed copy of Form PTO/SB/08a listing the Caldas document is again respectfully requested.

35 U.S.C. 102 – Novelty

A claim is anticipated only if each and every limitation as set forth in the claim is found, either expressly or inherently described, in a single prior art reference. *Verdegaal Bros. v. Union Oil Co. of Calif.*, 2 USPQ2d 1051, 1053 (Fed. Cir. 1987). The identical invention must be shown in as complete detail as is claimed. See *Richardson v. Suzuki Motor Co.*, 9 USPQ2d 1913, 1920 (Fed. Cir. 1989).

Claims 1, 3-4, 8 and 11-12 were rejected under Section 102(b) as allegedly anticipated by Hogset et al. (WO 02/44395). Applicants traverse.

Claim 1 is directed to a composition comprising a conjugate of a photosensitizer and a bacteriophage. Hogset lacks an explicit description of any such composition. At page 20, line 21, Hogset mentions that a photosensitizing agent may be optionally attached to, associated with, or conjugated to one or more carrier molecules, targeting molecules, or targeting vectors. Bacteriophages are listed as only one possible carrier in a long list of possibilities in a paragraph bridging pages 20 and 21. Moreover, Hogset's claim 18 merely refers to "one or both of the photosensitizing agent and the viral carrier" attached to, associated with, or conjugated to a carrier molecule, targeting molecule, or vector. The nature of the carrier is not further specified in any of the other claims. Note also that the carriers may be viral systems that include many more animal viruses (e.g., "adenovirus, lentiviruses and other retroviruses, adeno associated virus" at the bottom of page 20) than any specific bacteriophage. Further, all of Hogset's examples use a free photosensitizer (i.e., a photosensitizer that is not conjugated to any carrier, still less a bacteriophage). Indeed, Hogset emphasizes at page 12, line 11, that it is preferred that the photosensitizer is in free form (i.e., not conjugated to any other macromolecule).

Thus, Hogset merely suggests a number of possible carrier molecules that may be linked to either a photosensitizer or a viral carrier. Applicants respectfully submit that this does not constitute a clear or explicit description of a photosensitizer-bacteriophage conjugate as required by the present claim 1.

Therefore, Applicants' claimed invention does not lack novelty because the cited document does not disclose all limitations of independent claim 1. Moreover, the claims depending from claim 1 are also not anticipated by Hogset because the limitations of the independent claim are incorporated in their dependent claims. See *In re McCarn*, 101 USPQ 411, 413 (C.C.P.A. 1954).

Withdrawal of the Section 102 rejection is requested because the cited document fails to disclose all limitations of the claimed invention.

35 U.S.C. 103 – Nonobviousness

A claimed invention is unpatentable if the differences between it and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art. *In re Kahn*, 78 USPQ2d 1329, 1334 (Fed. Cir. 2006) citing *Graham v. John Deere*, 148 USPQ 459 (1966). The *Graham* analysis needs to be made explicitly. *KSR v. Teleflex*, 82 USPQ2d 1385, 1396 (2007). It requires findings of fact and a rational basis for combining the prior art disclosures to produce the claimed invention. See id. ("Often, it will be necessary for a court to look to interrelated teachings of multiple patents . . . and the background knowledge possessed by a person having ordinary skill in the art, all in order to determine whether there was an apparent reason to combine the known elements in the fashion claimed by the patent at issue"). The use of hindsight reasoning is impermissible. See id. at 1397 ("A factfinder should be aware, of course, of the distortion caused by hindsight bias and must be cautious of arguments reliant upon ex post reasoning"). Thus, a prima facie case under Section 103(a) requires "some rationale, articulation, or reasoned basis to explain why the conclusion of obviousness is correct." *Kahn* at 1335; see *KSR* at 1396. A claim that is directed to a combination of prior art elements "is not proved obvious merely by demonstrating that each of its elements was, independently, known in the prior art." Id. Finally, a determination of prima facie obviousness requires a reasonable expectation of success. See *In re Rinehart*, 189 USPQ 143, 148 (C.C.P.A. 1976).

Claims 1-5, 8-12 and 31 were rejected under Section 103(a) as allegedly unpatentable over Hogset et al. (WO 02/44395) in view of Embleton et al. (J. Antimicrobiol. Chemotherap. 50:857-864, 2002). Applicants traverse.

Hogset's disclosure was discussed above. Embleton describes a conjugate of antibody (IgG) and photosensitizer (SnCe6) for lethal photosensitization of *Staphylococcus aureus*. The latter document was discussed in the present specification at page 4, lines 5-11. Embleton's conjugate attaches to *S. aureus* through binding between the conserved IgG binding domains (i.e., the Fc region) and Protein A on certain *S. aureus* strains. Bacterial binding by Embleton's conjugate is not through an antigen-specific interaction between the variable antigen-binding IgG domains (i.e., the Fab region) and the staphylococcal bacterial surface as it appears the Examiner should believe for him to combine Hogset and Embleton. Neither cited document teaches or makes obvious an effective concentration of the conjugate's bacteriophage in Applicants' claimed composition (cf. the present claim 9). Embleton does not teach "the delivery of a wide range of pfu per injection site" as alleged by the Examiner in the Office Action at the top of page 7. It is totally silent on the use of bacteriophage as part of a photosensitizing conjugate.

The Examiner alleged that one of ordinary skill in the art would have found it obvious to replace the IgG with a staphylococcal bacteriophage from Hogset's disclosure. In this regard, the Examiner notes, "Hogset teaches that chlorin photosensitizer can be coupled with a bacteriophage to selectively target specific cell types." But as was previously discussed, Hogset does not actually describe any specific photosensitizer-bacteriophage conjugate, still less a chlorin-bacteriophage conjugate. And it should be stressed that Embleton's conjugate did not target specific bacteria by the IgG's binding of cognate antigen on staphylococcus bacteria. Instead, use of Embleton's conjugate was limited only to *S. aureus* (not any bacteria which is bound by a bacteriophage) and only those *S. aureus* strains that express Protein A because attachment is mediated between the Fc portion of IgG and the Protein A of *S. aureus*. IgG binding to specific bacterial antigen was not the targeting mechanism used by Embleton's conjugate. Thus, it is not analogous to replace Embleton's IgG by Hogset's carrier system.

Further, Hogset indicates that the carrier systems described therein (including bacteriophages) "do not generally have the ability to target the photosensitizing agent to specific cells" at page 21, lines 1-9. Therefore, the prior art actually teaches away from using a bacteriophage for targeting. Cf. new claims 34-36. Additionally, Hogset does not provide one of ordinary skill in the art with any information on targeting bacteria. Applicants' invention is concerned with photodynamic therapy (PDT) to kill bacteria. PDT involves treating an organism with a photosensitizer which, upon irradiation with light of a suitable wavelength, generates cytotoxic species that lyse bacteria (see page 2, line 30, to page 3, line 18 of the present specification). In contrast to Applicant's invention, Hogset relates to using a photosensitizer for delivery of a molecule into cells of a eukaryote (see page 6, lines 22-29) without killing the cells. Thus, since Hogset is concerned with types of cells other than bacteria and a delivery system into the cells' cytosol rather than killing them from the outside of a prokaryote, there is no teaching or suggestion that Hogset's methods could have been applied to the particular problems associated with targeting bacteria in PDT because Hogset is non-analogous art.

Finally, Applicants teach in their specification that the claimed invention relies on attachment of their conjugate to bacteria through specific binding by the conjugate's bacteriophage on a bacterial surface. Bacteriolysis by the bacteriophage is not needed. This unexpectedly results in broadening the range of usefulness of the claimed conjugate because many more bacteria are bound by bacteriophage than are necessarily lysed by those bacteriophage. See the present specification at page 4, lines 12-25, especially "It is known that although some bacteriophage will only kill a limited range of bacteria, they will bind to a broader range of bacteria. The present inventors have now found that some bacteriophage can serve as an effective, targeted delivery system for photosensitisers."

In summary, Hogset mentions a bacteriophage last among a long list of "carrier systems" in the context of delivering molecules into eukaryotic cells. Hogset does not teach anything about targeting bacteria and, in fact, teaches away from using bacteriophages for targeting cells. Thus, one of ordinary skill in the art would not have combined Hogset and Embleton as proposed in the Office Action, and would not have had any

expectation of success even had he done so. For the sake of argument, even if the Examiner were to maintain that Applicants' claimed invention is prima facie obvious, the unexpected result that their bacteriophage are useful for a broad range of bacteria and do not require bacteriolysis. Thus, Applicants' claimed invention is patentable. Also, no reasonable expectation of success is found in the prior art to use bacteriophage as a targeting system for a conjugate that kills bacteria through PDT instead of bacteriolysis.

Therefore, the combination of Hogset and Embleton does not render obvious Applicants' invention as represented by their independent claims. The dependent claims are also not rendered obvious by the two cited documents because all limitations of their independent claim are incorporated therein. M.P.E.P. § 2143.03 citing *In re Fine*, 5 USPQ2d 1596 (Fed. Cir. 1988).

Withdrawal of the Section 103 rejection is requested because the claims would not have been obvious to one of ordinary skill in the art when this invention was made.

Conclusion

Having fully responded to the pending Office Action, Applicants submit that the claims are in condition for allowance and earnestly solicit an early Notice to that effect. The Examiner is invited to contact the undersigned if additional information is required.

Respectfully submitted,

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